

SEQ ID NO:	PFAM NAME	DESCRIPTION	p-value	PFAM SCORE
	t			
429	zf-C3HC4	Zinc finger, C3HC4 type (RING finger)	8.6e-11	39.2
431	DEAD	DEAD/DRAH box helicase	1e-66	214.0
432	SH3	SH3 domain	3.4e-16	67.2
433	GTP_CDC	Cell division protein	2.1e-114	393.5
436	Collagen	Collagen triple helix repeat (20 copies)	4.6e-194	658.1
438	Ricin_B_lectin	Similarity to lectin domain of ricin b	0.0085	10.5
441	Alpha_adaptin_C	Alpha adaptin carboxyl-terminal domain	1.2e-256	866.0
442	Alpha_adaptin_C	Alpha adaptin carboxyl-terminal domain	1.8e-235	795.7
443	PDZ	PDZ domain (Also known as DHR or GLGF).	1.9e-65	230.9
445	LON	ATP-dependent protease La (LON) domain	0.00012	-17.1
446	ig	Immunoglobulin domain	0.00011	20.1
451	sushi	Sushi domain (SCR repeat)	1.4e-18	75.2
452	fn3	Fibronectin type III domain	1.5e-06	35.2
454	pyridoxal_dependent	Pyridoxal-dependent decarboxylase conse	8.3e-14	50.3
456	kinesin	Kinesin motor domain	4.9e-217	734.4
457	neur_chan	Neurotransmitter-gated ion-channel	1e-175	597.1
458	Josephin	Josephin	0.0002	18.7
468	bZIP	bZIP transcription factor	1.7e-07	31.8
470	NTP_transferase	Nucleotidyl transferase	6.3e-06	-26.3
471	WD40	WD domain, G-beta repeat	2e-28	107.9
473	LIM	LIM domain containing proteins	0.00021	20.7
477	zf-RanBP	Zn-finger in Ran binding protein and others.	0.028	21.0
479	WD40	WD domain, G-beta repeat	6.5e-18	73.0
480	KRAB	KRAB box	1e-31	118.8
481	ArfGap	Putative GTP-ase activating protein for Arf	8.4e-66	232.0
485	SH2	Src homology domain 2	0.011	11.4
486	Clq	Clq domain	4.3e-74	259.6
487	dsrm	Double-stranded RNA binding motif	1.1e-47	171.9
489	zf-C2H2	Zinc finger, C2H2 type	4.8e-153	521.9
490	Alpha_adaptin_C	Alpha adaptin carboxyl-terminal domain	3.4e-222	751.6
492	SKI	Shikimate kinase	1.2e-10	48.8
497	ENV_polyprotein	ENV polyprotein (coat polyprotein)	2.6e-22	77.6
498	abhydrolase_2	Phospholipase/Carboxylesterase	0.041	-48.1
500	rrm	RNA recognition motif.	5.4e-34	126.4
501	WW	WW domain	4.6e-18	73.4
502	ig	Immunoglobulin domain	1.1e-10	39.5
504	abhydrolase	alpha/beta hydrolase fold	0.045	-3.6
505	vwa	von Willebrand factor type A domain	7.1e-62	219.0
508	Na_K_ATPase_C	Na+/K+ ATPase C-terminus	2.3e-145	496.3
509	Exonuclease	Exonuclease	1.3e-56	201.5
510	Glycosyl_transf_1	Glycosyl transferases group 1	2.9e-06	27.0
511	Glycosyl_transf_1	Glycosyl transferases group 1	2.9e-06	27.0
512	Glycosyl_transf_1	Glycosyl transferases group 1	1.9e-09	38.5
514	pro_isomerase	Cyclophilin type peptidyl-prolyl cis-tr	1.8e-63	221.4

Polynucleotides encoding preferred polypeptide truncations of the invention can be used to generate polynucleotides encoding chimeric or fusion proteins comprising one or more domains of the invention and heterologous protein sequences.

5 The polynucleotides of the invention additionally include the complement of any of the polynucleotides recited above. The polynucleotide can be DNA (genomic, cDNA, amplified, or synthetic) or RNA. Methods and algorithms for obtaining such polynucleotides are well known to those of skill in the art and can include, for example, methods for determining hybridization conditions that can routinely isolate polynucleotides of the desired sequence identities.

10 In accordance with the invention, polynucleotide sequences comprising the mature protein coding sequences corresponding to any one of SEQ ID NO:1-1786 and 3573-5358, or functional equivalents thereof, may be used to generate recombinant DNA molecules that direct the expression of that nucleic acid, or a functional equivalent thereof, in appropriate host cells. Also included are the cDNA inserts of any of the clones identified herein.

15 A polynucleotide according to the invention can be joined to any of a variety of other nucleotide sequences by well-established recombinant DNA techniques (see Sambrook J et al. (1989) Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory, NY). Useful nucleotide sequences for joining to polynucleotides include an assortment of vectors, e.g., plasmids, cosmids, lambda phage derivatives, phagemids, and the like, that are well known in the art. Accordingly, the invention also provides a vector including a polynucleotide of the  
20 invention and a host cell containing the polynucleotide. In general, the vector contains an origin of replication functional in at least one organism, convenient restriction endonuclease sites, and a selectable marker for the host cell. Vectors according to the invention include expression vectors, replication vectors, probe generation vectors, and sequencing vectors. A host cell according to the invention can be a prokaryotic or eukaryotic cell and can be a unicellular  
25 organism or part of a multicellular organism.

The present invention further provides recombinant constructs comprising a nucleic acid having any of the nucleotide sequences of SEQ ID NO:1-1786 and 3573-5358 or a fragment thereof or any other polynucleotides of the invention. In one embodiment, the recombinant constructs of the present invention comprise a vector, such as a plasmid or viral vector, into  
30 which a nucleic acid having any of the nucleotide sequences of SEQ ID NO:1-1786 and 3573-5358 or a fragment thereof is inserted, in a forward or reverse orientation. In the case of a vector comprising one of the ORFs of the present invention, the vector may further comprise regulatory sequences, including for example, a promoter, operably linked to the ORF. Large numbers of suitable vectors and promoters are known to those of skill in the art and are commercially  
35 available for generating the recombinant constructs of the present invention. The following

vectors are provided by way of example. Bacterial: pBs, phagescript, PsiX174, pBluescript SK, pBs KS, pNH8a, pNH16a, pNH18a, pNH46a (Stratagene); pTrc99A, pKK223-3, pKK233-3, pDR540, pRIT5 (Pharmacia). Eukaryotic: pWLneo, pSV2cat, pOG44, PXTI, pSG (Stratagene) pSVK3, pBPV, pMSG, pSVL (Pharmacia).

- 5           The isolated polynucleotide of the invention may be operably linked to an expression control sequence such as the pMT2 or pED expression vectors disclosed in Kaufman et al., *Nucleic Acids Res.* 19, 4485-4490 (1991), in order to produce the protein recombinantly. Many suitable expression control sequences are known in the art. General methods of expressing recombinant proteins are also known and are exemplified in R. Kaufman, *Methods in*  
10 *Enzymology* 185, 537-566 (1990). As defined herein "operably linked" means that the isolated polynucleotide of the invention and an expression control sequence are situated within a vector or cell in such a way that the protein is expressed by a host cell which has been transformed (transfected) with the ligated polynucleotide/expression control sequence.

- Promoter regions can be selected from any desired gene using CAT (chloramphenicol  
15 transferase) vectors or other vectors with selectable markers. Two appropriate vectors are pKK232-8 and pCM7. Particular named bacterial promoters include lacI, lacZ, T3, T7, gpt, lambda PR, and trc. Eukaryotic promoters include CMV immediate early, HSV thymidine kinase, early and late SV40, LTRs from retrovirus, and mouse metallothionein-I. Selection of the appropriate vector and promoter is well within the level of ordinary skill in the art.
- 20   Generally, recombinant expression vectors will include origins of replication and selectable markers permitting transformation of the host cell, e.g., the ampicillin resistance gene of *E. coli* and *S. cerevisiae* TRP1 gene, and a promoter derived from a highly-expressed gene to direct transcription of a downstream structural sequence. Such promoters can be derived from operons encoding glycolytic enzymes such as 3-phosphoglycerate kinase (PGK), a-factor, acid  
25 phosphatase, or heat shock proteins, among others. The heterologous structural sequence is assembled in appropriate phase with translation initiation and termination sequences, and preferably, a leader sequence capable of directing secretion of translated protein into the periplasmic space or extracellular medium. Optionally, the heterologous sequence can encode a fusion protein including an amino terminal identification peptide imparting desired  
30 characteristics, e.g., stabilization or simplified purification of expressed recombinant product. Useful expression vectors for bacterial use are constructed by inserting a structural DNA sequence encoding a desired protein together with suitable translation initiation and termination signals in operable reading phase with a functional promoter. The vector will comprise one or more phenotypic selectable markers and an origin of replication to ensure maintenance of the  
35 vector and to, if desirable, provide amplification within the host. Suitable prokaryotic hosts for

transformation include *E. coli*, *Bacillus subtilis*, *Salmonella typhimurium* and various species within the genera *Pseudomonas*, *Streptomyces*, and *Staphylococcus*, although others may also be employed as a matter of choice.

As a representative but non-limiting example, useful expression vectors for bacterial use can comprise a selectable marker and bacterial origin of replication derived from commercially available plasmids comprising genetic elements of the well known cloning vector pBR322 (ATCC 37017). Such commercial vectors include, for example, pKK223-3 (Pharmacia Fine Chemicals, Uppsala, Sweden) and GEM 1 (Promega Biotech, Madison, WI, USA). These pBR322 "backbone" sections are combined with an appropriate promoter and the structural sequence to be expressed. Following transformation of a suitable host strain and growth of the host strain to an appropriate cell density, the selected promoter is induced or derepressed by appropriate means (e.g., temperature shift or chemical induction) and cells are cultured for an additional period. Cells are typically harvested by centrifugation, disrupted by physical or chemical means, and the resulting crude extract retained for further purification.

Polynucleotides of the invention can also be used to induce immune responses. For example, as described in Fan et al., *Nat. Biotech.* 17:870-872 (1999), incorporated herein by reference, nucleic acid sequences encoding a polypeptide may be used to generate antibodies against the encoded polypeptide following topical administration of naked plasmid DNA or following injection, and preferably intramuscular injection of the DNA. The nucleic acid sequences are preferably inserted in a recombinant expression vector and may be in the form of naked DNA.

#### 4.3 ANTISENSE

Another aspect of the invention pertains to isolated antisense nucleic acid molecules that are hybridizable to or complementary to the nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO:1-1786 and 3573-5358, or fragments, analogs or derivatives thereof. An "antisense" nucleic acid comprises a nucleotide sequence that is complementary to a "sense" nucleic acid encoding a protein, e.g., complementary to the coding strand of a double-stranded cDNA molecule or complementary to an mRNA sequence. In specific aspects, antisense nucleic acid molecules are provided that comprise a sequence complementary to at least about 10, 25, 50, 100, 250 or 500 nucleotides or an entire coding strand, or to only a portion thereof. Nucleic acid molecules encoding fragments, homologs, derivatives and analogs of a protein of any of SEQ ID NO:1787-3572 and 5359-7144 or antisense nucleic acids complementary to a nucleic acid sequence of SEQ ID NO:1-1786 and 3573-5358 are additionally provided.